

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1. (Currently amended) A method for providing a labeled target protein or labeled target peptide, which method comprises the steps of:

- a. contacting a chemical molecule, which chemical molecule comprises, ~~optionally beside a~~ spacer and/or linker residues, and optionally comprises the following parts:
 - a target protein or a target peptide residue which is covalently bound as one of both terminal groups of said chemical molecule to a chemical backbone, which chemical backbone consists of amino acids and/or spacers and optionally linkers, covalently bound to each other, and which backbone contains, ~~optionally beside a~~ spacer and/or linker residues, and optionally contains
 - one amino acid or spacer residue as the second of both terminal groups of said chemical molecule covalently bound to a reversible or irreversible affinity tagging residue, with the proviso that in case that the affinity tagging residue is an irreversible affinity tagging residue, there is at least one linker residue covalently bound to said amino acid or spacer residue, which amino acid or spacer residue is on the other hand covalently bound to the irreversible affinity tagging residue, and
 - one amino acid or spacer residue covalently bound to a labeling residue which labeling residue may be detected by physical means,with an affinity support, to obtain said chemical molecule bound to the affinity support via the affinity tag of the affinity tagging residue,
- b. removing impurities in the reaction mixture surrounding the affinity support to which the chemical molecule according to step a. is bound, and
- c. cleaving or eluting said chemical molecule from said affinity support to obtain
 - €1.(i) in case of an irreversible affinity tagging residue, a labeled target protein or labeled peptide comprising a chemical backbone, which backbone contains, ~~optionally beside a~~ spacer and/or linker residues, and optionally contains one amino acid or spacer residue covalently bound to a labeling residue which labeling residue may be detected by physical means,
 - €2.(ii) in case of a reversible affinity tagging residue, a chemical backbone covalently bound to a protein or a peptide residue, which backbone contains, ~~optionally beside a~~ spacer and/or linker residues, and optionally contains
 - one amino acid or spacer residue covalently bound to a labeling residue which labeling residue may be detected by physical means,

- one amino acid or spacer residue covalently bound to a labeling residue, which labeling residue may be detected by physical means, and which labeling residue or spacer residue is covalently bound to a reversible affinity tagging residue.

Claim 2. (Currently amended) A method for providing a labeled target protein or labeled target peptide, which method comprises a method of claim 1, comprising the steps of

~~1.a.~~ reacting a compound, which compound comprises, ~~optionally beside a said~~ spacer and/or linker residues, and optionally comprises the following parts

- one amino acid or spacer residue as one of both terminal groups of said chemical molecule covalently bound to a reversible or irreversible affinity tagging residue, with the proviso that in case that the affinity tagging residue is an irreversible affinity tagging residue, there is at least one linker residue covalently bound to said amino acid or spacer residue, which amino acid or spacer residue is on the other hand covalently bound to the irreversible affinity tagging residue,
- one amino acid or spacer residue covalently bound to a labeling residue which labeling residue may be detected by physical means,
- one amino acid or spacer residue covalently bound to a reactive group containing residue, which residue is covalently bound as one of both terminal groups of said compound, and wherein the reactive group is able to react with a functional group contained in a target protein or target peptide,

with a target peptide or target protein,

~~2.b.~~ contacting a chemical molecule obtained in step 1. with an affinity support, to obtain said chemical molecule bound to the affinity support via the affinity tag of the affinity tagging residue,

~~3.c.~~ removing impurities in the reaction mixture surrounding the affinity support to which the chemical molecule according to step a. is bound, and

[[4]].~~d.~~ cleaving or eluting said chemical molecule from said affinity support to obtain

[[4a.]](i) in case of an irreversible affinity tagging residue, a labeled target protein or labeled target peptide comprising a chemical backbone, which backbone contains, optionally beside spacer and/or linker residues, one amino acid or spacer residue covalently bound to a labeling residue which labeling residue may be detected by physical means,

[[4.b]](ii) in case of a reversible affinity tagging residue, a chemical backbone covalently bound to a protein or a peptide residue, which backbone contains, ~~optionally beside said~~ spacer and/or linker residues, and optionally contains

- one amino acid or spacer residue covalently bound to a labeling residue which labeling residue may be detected by physical means, and
- one amino acid or spacer residue covalently bound to a reversible affinity tagging residue.

Claim 3. (Currently amended) A compound, which compound comprises the following parts
 [[A]]a. a reactive group containing residue, which residue is covalently bound as one of both terminal groups of said compound, and wherein the reactive group is selected from the group consisting of thiol, halogen, imine, aldehyde, the double bond in a vinylsulfonyl or a maleimido group and a group which forms together with a carbonyl group of said residue a carboxylic acid derivative[[.]];

Bb. a label containing residue, which label may be detected by physical means[[.]];

Cc. an affinity tagging group containing residue, which residue is covalently bound as the second of both terminal residues in a CHEMICAL COMPOUND, and wherein said affinity tagging group is a reversible affinity tagging group or an irreversible affinity tagging group, with the proviso that in case that the affinity tagging group is an irreversible affinity tagging group, there is at least one linker residue covalently bound to an amino acid or spacer residue, which carries the irreversible affinity tagging group, and

which residue of any of ~~A., B. or C.~~ a., b., or c. is selected from

- 1 to 10 amino acids, which amino acids are covalently bound to each other via amide bonds of the carboxylic acid group of one amino acid and the amine group of a second amino acid,
- 1 to 10 spacers, which spacers are covalently bound to each other via functional groups of said spacers, and
- 1 to 10 amino acids and spacers, which amino acid and spacers are covalently bound to each other either via amide bonds of the carboxylic acid group of one amino acid and the amine group of a second amino acid, or via functional groups of said spacers, or via an amine group or a carboxylic acid group of an amino acid with a functional group of a spacer[[.]];

Dd. optionally further spacer residues[[.]]; and

Ee. optionally linker residues.

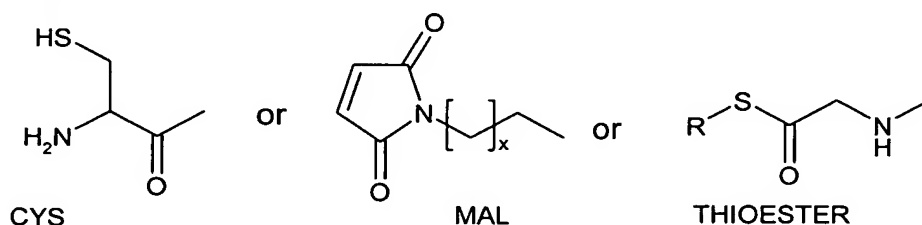
Claim 4. (Original) A compound according to claim 3, which is a compound of formula



wherein

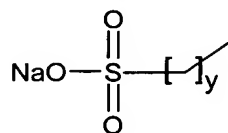
A is

a group of formula



wherein x is 1 to 5, and

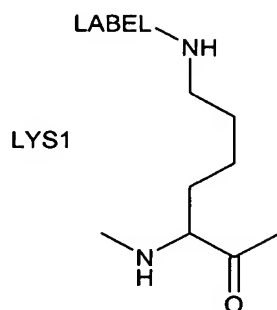
R is (C₁₋₄)alkyl carboxylic acid ester, e.g. propionic acid ethyl ester, or a group of formula



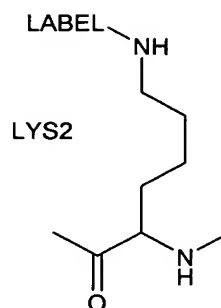
wherein y is 2 to 4, e.g. 2;

D is

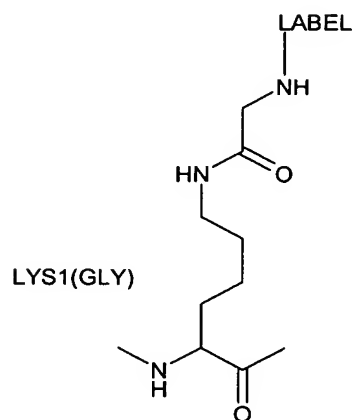
a group of formula



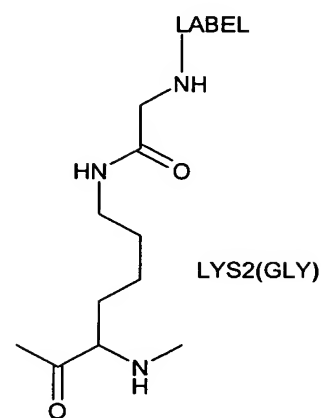
or



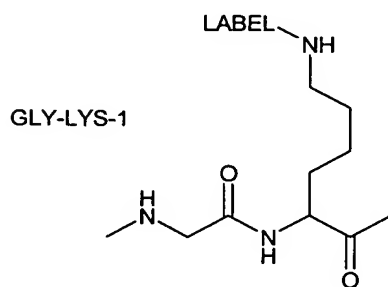
or a group of formula



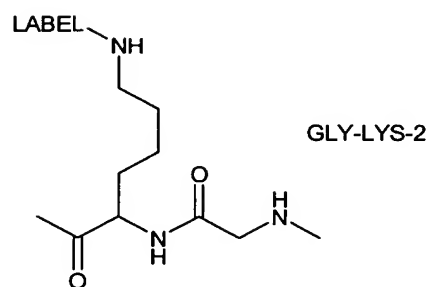
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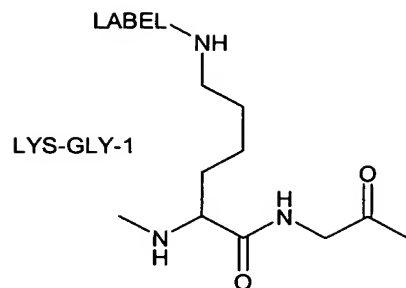
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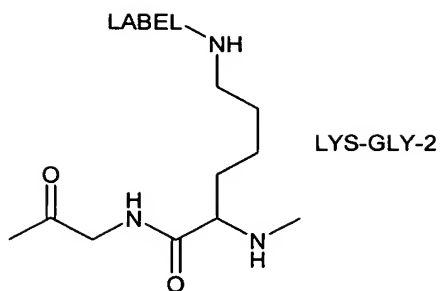
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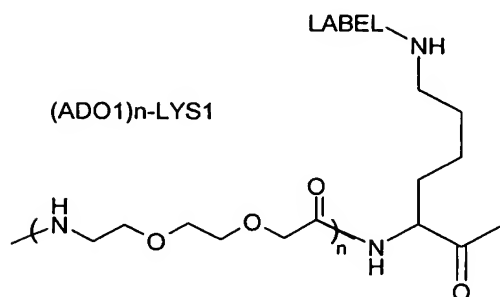
or a group of formula



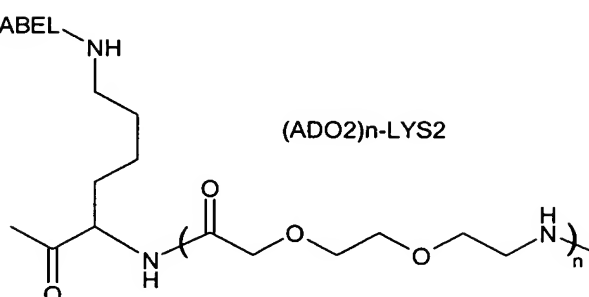
or



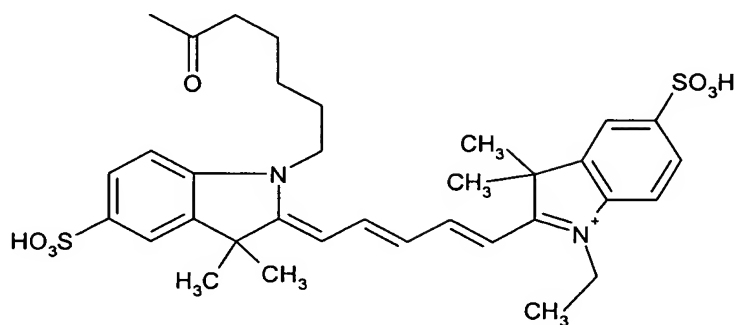
or a group of formula



or

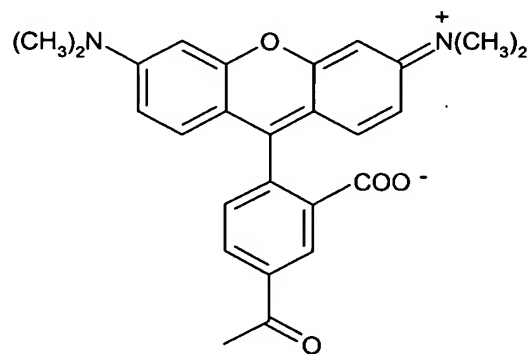


LABEL is a group of formula



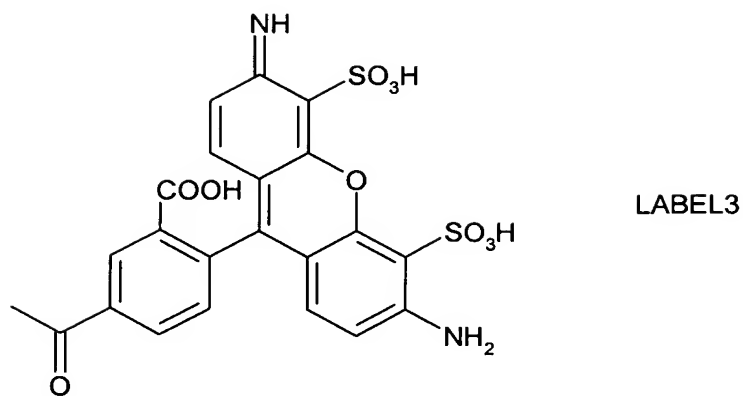
LABEL1
and
LABEL 4

or a group of formula

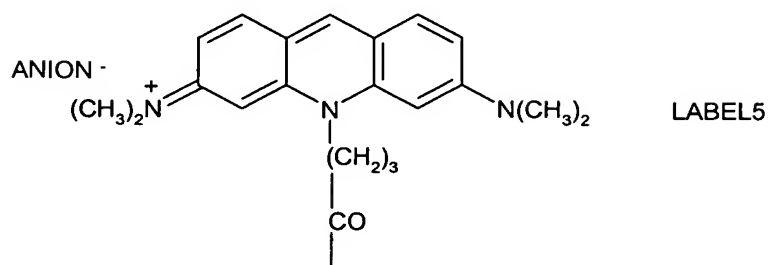


LABEL2

or a group of formula

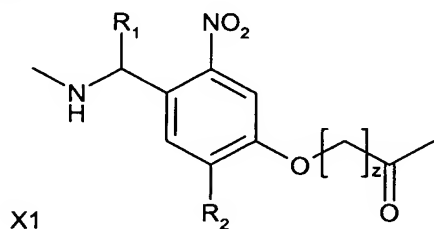


or a group of formula

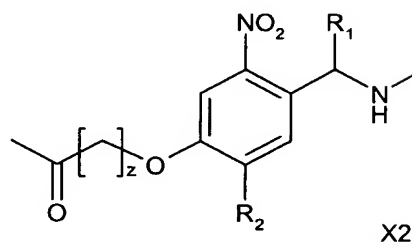


wherein ANION is a negatively charged group, e.g. an anion, such as CF_3COO^- ,

X is a group of formula



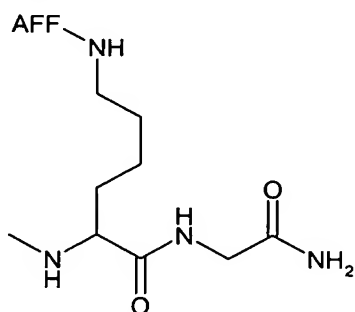
or



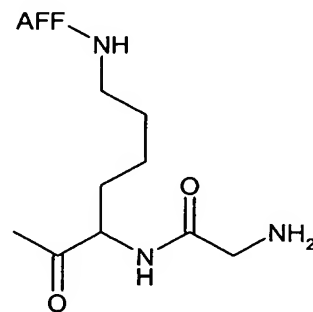
wherein

R_1 is H or CH_3 , R_2 is H or $-\text{OCH}_3$ and z is 1 to 5;

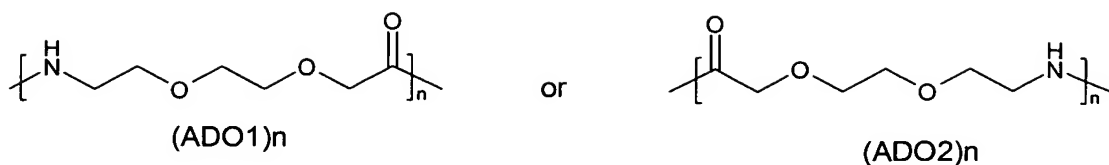
E is a group of formula



or



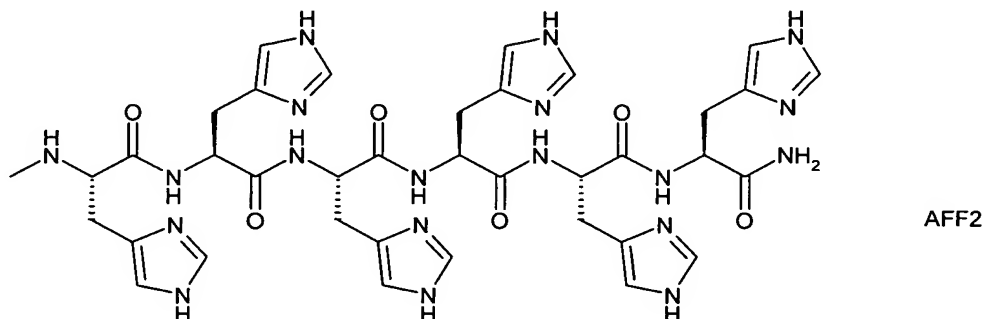
or a group of formula



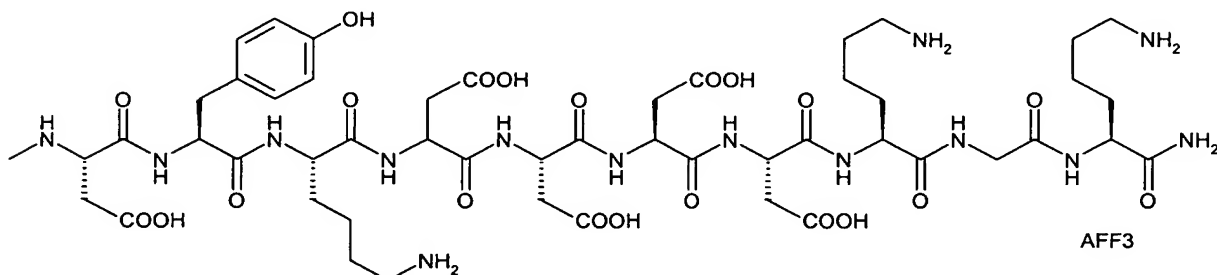
wherein to one of the amine groups a group AFF is bound and wherein n is 1 to 4,

and

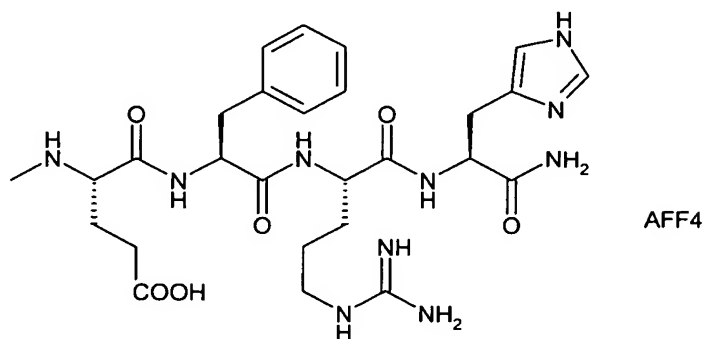
EITHER the affinity tag is bound to a carboxylic acid residue, e.g. the carboxylic residue of (ADO1)_n and is a group of formula



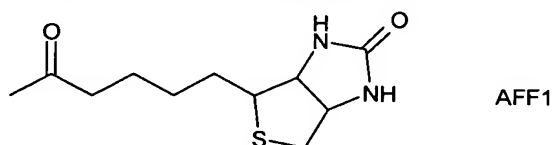
or of formula



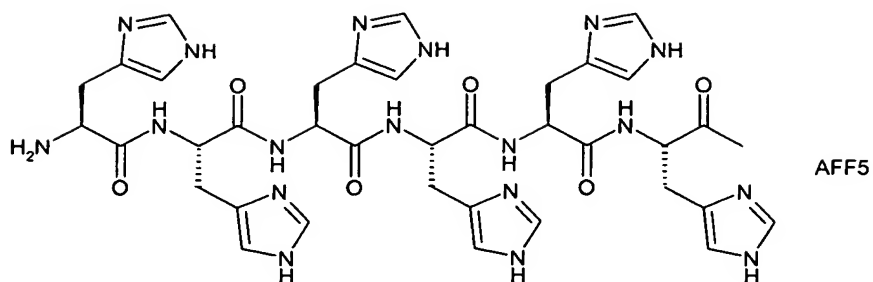
or of formula



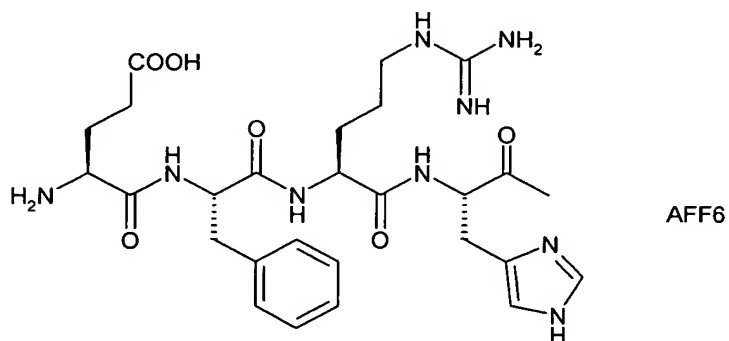
OR the affinity tag is bound to an amino group, e.g. to the ε-amino group of the lysine residue in LYS-GLY-NT1 or LYS-GLY-NT2; or to an amino group of (ADO1)_n and is a group of formula



or of formula

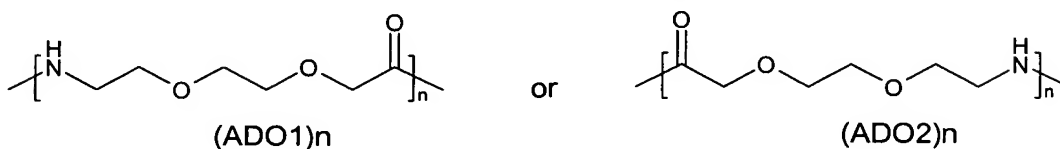


or of formula



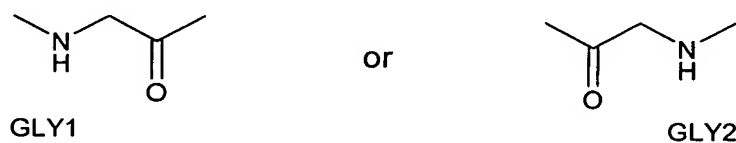
and

Y, Y', Y'' independently of each other are a group of formula



wherein n is 1 to 4,

or a group of formula



with the proviso, that

- IF A is CYS or MAL,

THEN

D is LYS1, LYS1(GLY), GLY-LYS1, LYS-GLY1 or (ADO1)_n-LYS1,

X is X1,

E is LYS-GLY-NT1 or (ADO1)_n,

AFF is AFF1, AFF2, AFF3 or AFF4, and

Y, Y' and Y'' independently of each other are GLY1 or (ADO1)_n, wherein n is 1 to 4,

and

- IF A is THIOESTER,

THEN

D is LYS2, GLY-LYS1, LYS-GLY2 or (ADO2)_n-LYS1,

X is X2,

E is LYS-GLY-NT2 or (ADO2)_n and n is 1 to 4,

AFF is AFF1, AFF5 or AFF6, and

Y, Y' and Y'' independently of each other are GLY2 or (ADO2)_n, wherein n is 1 to 4.

Claim 5. (Currently amended) A compound of ~~of~~ according to claims 3-4 wherein A, Y, D, Y', X, Y'' and E are as defined in TABLE 1 below, wherein in X1 and X2, R₁ is methyl, R₂ is methoxy and z=3, and in (ADO1)_n and (ADO2)_n n=1, except for EX 12 wherein n=3; and for EX 11, 15, and 26 to 29 wherein n=2:

TABLE 1

EX	A	Y	D	LABEL	Y'	X	Y''	E	AFF
8	CYS	GLY1	LYS1	LABEL1	GLY1	X1	ADO1	LYS-GLY-NT1	AFF1
9	CYS	GLY1	LYS1	LABEL2	GLY1	X1	ADO1	LYS-GLY-NT1	AFF1
10	CYS	GLY1-ADO1	ADO1-LYS1	LABEL1	GLY1	X1	ADO1	LYS-GLY-NT1	AFF1
11	CYS	GLY1	LYS1	LABEL1	GLY1	X1	(ADO1) ₂	LYS-GLY-NT1	AFF1
12	CYS	GLY1	LYS1	LABEL1	GLY1	X1	(ADO1) ₃	LYS-GLY-NT1	AFF1
13	CYS	GLY1	LYS1	LABEL1	GLY1	X1	---	ADO1	AFF2
14	CYS	GLY1	LYS1	LABEL1	GLY1	X1	ADO1	ADO1	AFF2
15	CYS	GLY1	LYS1	LABEL1	GLY1	X1	(ADO1) ₂	ADO1	AFF2
16	CYS	GLY1-GLY1	LYS1 (GLY)	LABEL2	GLY1	X1	ADO1	LYS-GLY-NT1	AFF1
17	CYS	GLY1	LYS1	LABEL1	GLY1	---	ADO1	ADO1	AFF3
18	CYS	GLY1	LYS1	LABEL1	GLY1	X1	---	ADO1	AFF3
19	CYS	GLY1	LYS1	LABEL1	GLY1	X1	ADO1	ADO1	AFF3
20	CYS	GLY1	LYS1	LABEL3	GLY1	X1	ADO1	ADO1	AFF2
21	CYS	GLY1	LYS1	LABEL4	GLY1	X1	ADO1	ADO1	AFF4
22	MAL	GLY1-GLY1	LYS1	LABEL4	GLY1	X1	ADO1	ADO1	AFF4
23	CYS	GLY1	LYS1	LABEL5	GLY1	X1	ADO1	ADO1	AFF2
24	CYS	GLY1	LYS1	LABEL3	GLY1	---	ADO1	ADO1	AFF2
25	CYS	GLY1	LYS1	LABEL1	GLY1	---	ADO1	ADO1	AFF2
26	THIOESTER; R= (CH ₂) ₂ -CO-OEt	GLY2	LYS2	LABEL1	GLY2	X2	(ADO2) ₂	LYS-GLY-NT2	AFF1
27	THIOESTER R= (CH ₂) ₂ -CO-OEt	GLY2	LYS2	LABEL5	GLY2	X2	(ADO2) ₂	LYS-GLY-NT2	AFF1
28	THIOESTER R= (CH ₂) ₂ -SO ₃ H	GLY2	LYS2	LABEL1	GLY2	X2	(ADO2) ₂	LYS-GLY-NT2	AFF1
29	THIOESTER R= (CH ₂) ₂ -SO ₃ H	GLY2	LYS2	LABEL5	GLY2	X2	(ADO2) ₂	LYS-GLY-NT2	AFF1
30	THIOESTER	GLY2	LYS2	LABEL5	GLY2	X2	ADO2	ADO2	AFF5

EX	A	Y	D	LABEL	Y'	X	Y''	E	AFF
	R= (CH ₂) ₂ -CO-OEt								
31	THIOESTER R= (CH ₂) ₂ -CO-OEt	GLY2	LYS2	LABEL1	GLY2	X2	ADO2	ADO2	AFF5
32	THIOESTER R= (CH ₂) ₂ -SO ₃ H	GLY2	LYS2	LABEL1	GLY2	X2	ADO2	ADO2	AFF6
33	MAL	GLY1	GLY-LYS1	LABEL2	GLY1	X1	ADO1	LYS-GLY-NT1	AFF1

and wherein the groups

CYS, MAL, THIOESTER, GLY1, GLY2, LYS1, LYS1(GLY), LYS2, LABEL1, LABEL2, LABEL3, LABEL4, LABEL5, X1, X2, (ADO1)_n, (ADO2)_n, LYS-GLY-NT1, LYS-GLY-NT2, AFF1, AFF2, AFF3, AFF4, AFF5 and AFF6 are as defined in claim 4.

Claim 6. (Currently amended) A compound ~~of any one of~~ according to claims 3 ~~to 5~~, which is covalently bound to the residue of a target protein or a target peptide via a bond originating from the reaction of a reactive group ~~as defined in any one of claims 3 to 4~~, with a functional group of said target protein or target peptide.

Claim 7. (Currently amended) A compound ~~of~~ according to claim 6, which compound is further bound to an affinity support via ~~the~~ an affinity tagging group ~~defined in any one of claims 3 or 4~~.

Claim 8. (Currently amended) A compound ~~of any one of~~ according to claims 3 ~~to 7~~ in the form of a salt.

Claim 9. (Currently amended) A compound ~~of any one of~~ according to claims 3 ~~to 5 or 8~~, when ~~dependent on claims 3 to 5~~, bound to a solid support via a terminal functional group.

Claim 10. (Currently amended) The use of a compound ~~of any one of~~ according to claims 3 ~~to 5 or 8~~, when ~~dependent on claims 3 to 5~~, for the labeling of a target protein or target peptide.

Claim 11. (Original) The use of a target protein or target peptide bound to a compound according to claim 6, in a high throughput screening assay.

Claim 12. (Currently amended) A kit comprising a compound ~~of~~ of claims 3 ~~to 5 or 8~~, when ~~dependent on claims 3 to 5~~, or a compound ~~according to any one of claims 6 or 8~~, when ~~dependent on claim 6~~, and instructions for using the kit.

Claim 13. (Currently amended) A method for identifying an agent that modulates the activity or characteristic of a target protein or a target peptide comprising the steps

- a. contacting a target protein or target peptide bound to a compound according to claim 6, with a candidate compound, which is expected to modulate the activity or characteristics of said target protein or target peptide,
- b. measuring a signal,
~~b1-(i)~~ in the absence of such candidate compound, and
~~b2-(ii)~~ in the presence of such candidate compound
and determining whether there is a difference in the signals measured in steps ~~b1-~~ and ~~b2-(i)~~
and ~~(ii)~~, and
- c. choosing an agent determined in step b.

Claim 14. (Original) A pharmaceutical composition comprising an agent identified in a method of claim 13 in association with at least one pharmaceutical excipient, e.g. appropriate carrier and/or diluent, e.g. including fillers, binders, disintegrators, flow conditioners, lubricants, sugars and sweeteners, fragrances, preservatives, stabilizers, wetting agents and/or emulsifiers, solubilizers, salts for regulating osmotic pressure and/or buffers, e.g. further comprising another pharmaceutically active agent.

Claim 15. (Original) An agent identified by a method of claim 13 for use as a pharmaceutical.

Claim 16. (Original) A method of treatment disorders mediated by a target protein or target peptide in vivo, comprising administering to a subject in need of such treatment an effective amount of an agent identified by a method according to the present invention.

Claim 17. (New) A kit comprising a compound of claim 6, and instructions for using the kit.